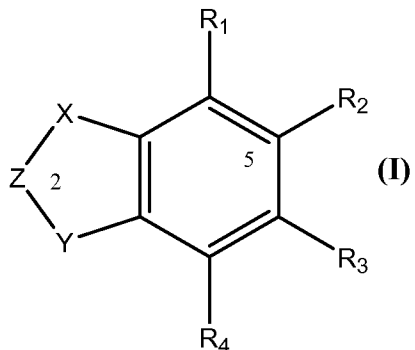


Claims Listing

1. (Currently amended) A method of inhibiting ~~cytokine or biological~~ activity of MIF comprising contacting MIF with ~~a cytokine or biological~~ an MIF activity-inhibiting effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof



wherein

X is—N(R₆)—;

Y is—N(R₇)—;

Z is—C(O)—;

R₁ is selected from hydrogen, or (CR₅R_{5'})_nhalo;

R₂ is selected from the group consisting of C₁-C₂₀alkyl, C₂-C₂₀alkenyl, C₂-C₂₀alkynyl, (CR₁₂R_{12'})_mC(O)R₈, (CR₁₂R_{12'})_mC(S)R₈, (CR₁₂R_{12'})_mS(O)R₈, (CR₁₂R_{12'})_mS(O)₂R₈, (CR₁₂R_{12'})_mOR₉, (CR₁₂R_{12'})_mSR₉, (CR₁₂R_{12'})_nNR₁₀R₁₁, (CR₁₂R_{12'})_mC(=NR₂₄)R₂₂ and (CR₁₂R_{12'})_mR₁₃;

R₃ is selected from hydrogen, C₁-C₆alkyl, (CR₁₆R_{16'})_pNR₁₄R₁₅, (CR₁₆R_{16'})_pOR₁₇, (CR₁₆R_{16'})_phalo, and (CR₁₆R_{16'})_pNO₂

SECOND AMENDMENT AND RESPONSE TO OFFICE ACTION
U.S.S.N. 10/517,264

R₄ is hydrogen, or halogen;

Each R₅ and R₅ is independently hydrogen,

R₆ is hydrogen, or C₁-C₃alkyl;

R₇ is hydrogen or C₁-C₃alkyl;

R₈ is selected from the group consisting of hydrogen, C₁-C₂₀alkyl, C₂-C₂₀alkenyl, C₂-C₂₀alkynyl, OR₁₉, SR₁₉, N(R₂₀)₂, [NH—CH(R₂₁)—C(O)]_q—OR₂₉, pyranosyl and (CR₁₂R_{12'})_tR₁₃;

R₉ is hydrogen;

R₁₀ and R₁₁ are independently selected from hydrogen, and C(O)R₂₃;

Each R₁₂ and R_{12'} is independently hydrogen;

R₁₃ is selected from OR₂₅, SR₂₅, halo, N(R₂₅)₂, and C(O)R₃₁;

R₁₄ and R₁₅ are each hydrogen;

Each R₁₆ and R_{16'} is hydrogen;

R₁₇ is hydrogen;

R₁₉ and each R₂₀ are independently selected from hydrogen, C₁-C₂₀alkyl, and, (CR₂₆R_{26'})_tR₂₇;

R₂₁ is the characterising group of an amino acid wherein the amino acid is alanine, phenylalanine, serine, homoserine or norvaline;

R₂₂ is NH(C₁₋₆alkyl);

R₂₃ is (CR₂₆R_{26'})_tR₂₇;

SECOND AMENDMENT AND RESPONSE TO OFFICE ACTION
U.S.S.N. 10/517,264

Each R_{24} is independently selected from hydrogen and C_1 - C_6 alkyl;

Each R_{25} is independently selected from hydrogen, and C_1 - C_6 alkyl;

Each R_{26} and $R_{26'}$ is independently hydrogen;

R_{27} is selected from, OR_{30} , SR_{30} , and aryl;

Each R_{29} is independently selected from hydrogen and C_1 - C_3 alkyl;

Each R_{30} is independently selected from, C_1 - C_3 alkyl, and heterocyclyl;

R_{31} is heterocyclyloxy;

n is 0 or an integer from 1 to 3;

m is 0 or an integer from 1 to 20;

p is 0 or an integer from 1 to 6;

q is an integer from 1 to 5;

t is an integer from 1 to 10;

wherein alkyl, alkenyl, alkynyl, aryl and heterocyclyl may be optionally substituted.

2. (Previously presented) A method according to claim 1 wherein X is—N(H)—, Y is —N(H)—, and Z is —C(O)—.

Claims 3 - 17 (Cancelled)

18. (Original) A method according to claim 1 wherein the compound of formula 1 is selected from the group consisting of: benzimidazole-2-one-5-n-pentanoate, 5-[2-(1-oxy-2-hydroxyethyl)ethyl]benzimidazol-2-one-5-carboxylate, benzimidazole-2-one-5-methanoate, benzimidazole-2-one-5-ethanoate, 3,4,5-tris(acetyloxy)-6-[(acetyloxy)methyl]tetrahydro-2H-pyran-2-yl-benzimidazole-2-one-5-carboxylate, 5-bromo-6-methylbenzimidazol-2-one, 5-hydroxy-6-methylbenzimidazol-2-one, 5-dodecanylbenzoimidazol-2-one, 4,5,7-tribromo-6-methylbenzimidazol-2-one, 4,5,6,7-tetrabromobenzimidazol-2-one, 5-methyl-6-nitrobenzimidazol-2-one, 5-amino-6-methylbenzimidazol-2-one, N-(6-methylbenzimidazol-5-yl)-2-pyrimidin-2-yl-sulfanyl-acetamide, pentyl-benzimidazol-2-one-5-carbothioate, 5-(benzimidazol-2(3H)-one-6-yl)-5-oxopentanoic acid, 2(3H)-benzimidazolone-5-sulfonic acid pentyl ester, 2(3H)-benzimidazolone-5-sulfonic acid pentyl amide, N-butyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazole-5-carboximidamide, 5-heptanoylbenzofuran-2(3H)-one, methyl 3-hydroxy-2-{[(2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-yl)carbonyl]amino}propanoate, 3-hydroxy-2-{[(2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-yl)carbonyl]amino}propanoic acid, methyl 2-{[(2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-yl)carbonyl]amino}-3-phenylpropanoate, 2-{[(2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-yl)carbonyl]amino}-3-phenylpropanoic acid, and N-(3,4-dihydroxyphenethyl)-2-oxo-2,3-dihydro-1H-1,3-benzimidazole-5-carboxamide.

19. (Currently amended) A method of treating, ~~preventing~~ or diagnosing ~~a disease or condition~~ rheumatoid arthritis wherein MIF ~~cytokine or biological~~ activity is implicated comprising the administration of a treatment, ~~prevention~~ or diagnostic effective amount of a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt thereof to a

subject in need thereof.

Claims 20-22. (cancelled)

23. (Original) A method of claim 19 wherein the subject is a human subject.

Claims 24-25. (cancelled)

26. (Currently amended) A method of treating ~~or preventing a disease or condition~~ rheumatoid arthritis wherein MIF ~~cytokine or biological~~ activity is implicated comprising:
administering to a mammal a compound of formula (I) as defined in claim 1 or a
pharmaceutically acceptable salt thereof and a second therapeutic agent.

27. (original) A method according to claim 26 wherein the second therapeutic agent is
a glucocorticoid.

28. (Currently amended) A method of ~~prophylaxis or treatment of a disease or condition~~ rheumatoid arthritis for which treatment with a glucocorticoid is indicated, said
method comprising: administering to a mammal a glucocorticoid and a compound of formula (I)
as defined in claim 1 or a pharmaceutically acceptable salt thereof.

29. (Currently amended) A method of treating a steroid-resistant ~~disease or condition~~ rheumatoid arthritis comprising: administering to a mammal a glucocorticoid and a compound of

formula (I) as defined in claim 1 or a pharmaceutically acceptable salt thereof.

Claims 30-40. (Cancelled)

41. (Previously presented) A method according to claim 1 wherein

R_1 is hydrogen or $(CR_5R_{5'})_n\text{halo}$;

R_2 is selected from $C_{1-20}\text{alkyl}$, $(CR_{12}R_{12'})_mC(O)R_8$, $(CR_{12}R_{12'})_mS(O)_2R_8$, $(CR_{12}R_{12'})_nNR_{10}R_{11}$, $(CR_{12}R_{12'})_mC(=NR_{24})R_{22}$ and $(CR_{12}R_{12'})_mR_{13}$;

R_3 is selected from hydrogen, $C_{1-6}\text{alkyl}$, $(CR_{16}R_{16'})_pNR_{14}R_{15}$, $(CR_{16}R_{16'})_pOR_{17}$, $(CR_{16}R_{16'})_p\text{halo}$ and $(CR_{16}R_{16'})_pNO_2$;

R_4 is hydrogen or halogen;

Each R_5 and $R_{5'}$ is independently hydrogen;

R_8 is selected from $C_1\text{-}C_{20}\text{alkyl}$, OR_{19} , SR_{19} , $N(R_{20})_2$, $[NH\text{-}CH(R_{21})\text{-}C(O)]_q\text{-}OR_{29}$, pyranosyl and $(CR_{12}R_{12'})R_{13}$;

R_9 is hydrogen;

R_{10} and R_{11} are independently selected from hydrogen and $C(O)R_{23}$;

Each R_{12} and $R_{12'}$ is independently hydrogen;

R_{13} is selected from OR_{25} , SR_{25} , halo, $N(R_{25})_2$ and $C(O)R_{31}$;

R_{14} and R_{15} are each hydrogen;

Each R_{16} and $R_{16'}$ is hydrogen;

R_{17} is hydrogen;

R_{19} and each R_{20} are independently selected from hydrogen, $C_1\text{-}C_{20}\text{alkyl}$, and $(CR_{26}R_{26'})_tR_{27}$;

R_{21} is the characterising group of phenylalanine or serine;

R_{22} is $NH(C_{1-6}\text{alkyl})$;

SECOND AMENDMENT AND RESPONSE TO OFFICE ACTION
U.S.S.N. 10/517,264

R_{23} is $(CR_{26}R_{26'})_tR_{27}$;

Each R_{24} is independently selected from hydrogen and C_1 - C_6 alkyl;

Each R_{25} is independently selected from hydrogen and C_1 - C_6 alkyl;

Each R_{26} and $R_{26'}$ is independently hydrogen;

R_{27} is selected from OR_{30} , SR_{30} and aryl;

Each R_{29} is independently selected from C_1 - C_3 alkyl and heterocyclyl; and

R_{31} is heterocycloxy.

42. (Previously presented) A method according to claim 41 wherein

n is 0;

m is 0;

p is 0;

q is 0; and

t is 1 or 2.

43. (Previously presented) A method according to claim 1 wherein the compound of formula (I) is benzimidazole-2-one-5-n-pentanoate.